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CHANGES IN THE MORPHOLOGICAL COMPOSITION OF THE PERIPHERAL BLOOD OF DOGS OF VARIOUS HIGHER NERVOUS ACTIVITY TYPES UNDER THE INFLUENCE OF CHRONIC IRRADIATION WITH SMALL DOSES OF GAMMA RAYS (COO)

[Following is a translation of an article by 0. F. Makarchenko, M. F. Sirotina, and R. S. Zlatin in Fiziologichnyy Zhurnal (Physiology Journal), Vol. V, No. 6, 1959, pages 769-773.]

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The problem of the influence of chronic irradiation of animals with small doses of ionizing radiation on the functional status of the organs and systems of organs is of great theoretical and practical importance. Considerable interest is aroused by studies of the influence of so-called maximum permissible doses, which still require establishment of the necessary physiological foundation. This has been caused by the extensive use of atomic energy for peaceful purposes, and also by the increase of the natural background of radiation in recent times.

In connection with this circumstance, we have studied the changes in the morphologic composition of the peripheral blood in dogs with previously known typological features of higher nervous activity under the influence of chronic irradiation with small, maximum permissible doses of gamma-rays from radioactive cobalt (Co<sup>60</sup>). We have also studied changes in the higher nervous activity (Makarchenko and Zlatin, 1959).

We carried out complete hematologic studies: determinations of the percentage composition of hemoglobin, erythrocyte counts, determinations of the absolute numbers of neutrophylic leukocytes, lymphocytes, eosinophils, and monocytes, and a determination of the ESR. The animals were exposed to total irradiation daily except Sundays for a period of six years. The daily dose was 0.05 r.

Under observation we had seven dogs, from which — we drew blood several times over a period of more than a year in order to determine the baseline hematologic norms. Subsequently, four dogs (Tuzik, Metis, Dzhul'bars, and Ryabchik) were exposed to chronic irradiation (in this article we are presenting the results of irradiation over a period of a year). The other three dogs (Erik, Byel'chik, and Mak) served as controls. The conditions of maintenance, feeding, and the like were identical for the experimental and the control dogs.

The experimental dogs were characterized by the following: Metis - a male, mixture of shepherd and mastiff, was six years of age and weighed 25 kg. This dog was of the strong type of nervous activity with predominance of the stimulatory over the inhibitory process. Tuzik - a male, mixture of mastiff and greyhound, was five years of age, weighed 26 kg, and was of the strong, unequilibrated type. Dzhul'bars - a male, mastiff, was seven years of age, weighed 25 kg, and was of the intermediate type of nervous activity, with predominance of the stimulatory over the inhibitory process. Ryabchik - a male, mastiff, was ten or eleven years of age, weighed 21 kg, and was of the weak type.

The control dogs were characterized by the following: Erik - a male, mastiff, was 3.5 to four years of age, weighed 23 kg, and was of the strong, unequilibrated type. Byel'chik - a male, mastiff, was ten or eleven years of age, weighed 11 kg, and was of the intermediate type. Mak - a male, shepherd, was seven years of age, weighed 26 kg, and was of the weak type of higher nervous activity.

Studies have recently appeared in the literature in which reports are presented on changes in the morphologic composition of the blood in persons exposed during their daily work to the chronic influence of small doses of ionizing radiation (Fateyeva, 1955; Morozov, 1957; Kuznetsov, 1957; Kovnatskyy, 1956; Kozlova, 1957; Danilin, 1958;

Karter, 1952, and others). It should be noted that, in the majority of these studies, there were no baseline hematologic data prior to exposure to radiation, the doses of radiation were not expressed precisely, and other hematologic diseases of a chronic nature were not always excluded, although these are strongly reflected in the composition of the blood.

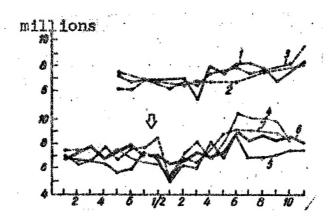


Fig. 1. Changes in the erythrocyte count.

The upper part of the drawing refers to the control dogs, the lower part to the experimental dogs. The horizontal scale represents months of irradiation, the vertical scale the erythrocyte count in millions. Curve 1 is dog Erik, 2 is dog Mak, 3 is dog Byel'chik, 4 is Dzhul'bars, 5 is Metis, 6 is Ryabchik, 7 is Tuzik. Arrow indicates the onset of irradiation.

Experimental findings showing the course of the changes in the blood in healthy animals upon exposure to precise doses of radiation are relatively sparse in the literature. Byeloborodova and Baranova (1957), during a period of internal irradiation of rabbits with small doses of radioactive cesium (10.6 microcuries/kg), demonstrated a number of symptoms which testify to the presence of early forms of disruption in hematopoiesis. These same authors studied disturbances in the lymphatic system and in erythropoiesis during a two-year daily administration to rabbits of radioactive ruthenium in doses

of 3.9 microcuries/kg. Significant disturbances in the blood system were demonstrated by Byeloborodova and Baranova (1957) upon administration of relatively small doses of strontium (2.68 microcuries/kg). It should be pointed out that the authors observed death in a high number of the animals exposed to prolonged irradiation with \$r89 (36 months), and systematically studied the peripheral blood, showing that signs of disordered hematopoiesis appear in a regular sequence: during the early period of the studies (11 to 12 months), there is great lability in the blood indices, and, in the later period (11 to 24 months), there is deterioration.

Very interesting are the findings of LaptevaPopova (1957, 1958) who, for a period of five years, observed changes in the bone marrow and peripheral blood in
a group of dogs which were systematically irradiated with
X-rays in doses of five to ten r. This author reports a
marked disturbance in the composition of the blood, along
with the emergence of leukoses in a number of instances.
The duration of these experiments enabled Lapteva-Popova
to divide the reaction of the hematopoietic system into
a series of periods: (a) lability of the hematopoietic
functions, (b) suppression of these functions, (c) temporary adaptation to the injurious factor, and (d) terminal
period. The duration and sequence of the periods, the author points out, are closely connected with the size of the
dose of radiation, the individual peculiarities of the animals, and their resistance.

Findings on changes in the composition of the blood upon chronic exposure to ionizing radiation, with account being taken of the type of higher nervous activity of animals, have not been discovered in the literature at our disposal.

Our first studies were performed 15 days after the onset of irradiation. Later, every month, counting from the day after the onset of exposure to ionizing radiation, we drew blood for complete hematologic analysis. At these times, studies of hematologic indices of the control animals were also made for comparative purposes.

Two weeks after the onset of irradiation, we observed the appearance of a marked reaction, in the form of

Tchanges in the leukocyte count, in only two of the experimental animals: Tuzik and Metis - dogs of the strong type of higher nervous activity. In Metis, there was a marked increase in the leukocyte count (9600 up to 17,600); in Tuzik, on the contrary, it decreased (13,200 down to 9600). In the other two dogs - Dzul'bars and Ryabchik - we did not notice any essential changes in the blood indices.

With continued irradiation, particular interest is attached to the changes in the elements of the red blood (Fig. 1).

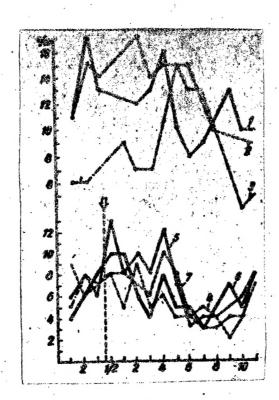


Fig. 2. Changes in the reticulocyte counts.

Vertical scale represents the number of reticulocytes in percent. The other labels are the same as in Fig. 1.

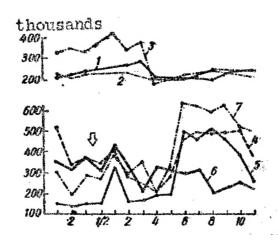


Fig. 3. Changes in the thrombocyte counts.

Vertical scale represents the number of thrombocytes in thousands. The other designations are the same as in Fig. 1.

A month after the onset of irradiation, all animals except Ryabchik (the weak type) exhibited a marked reduction in the erythrocyte count. By the end of the second or third month, the erythrocyte counts reverted to their original levels; furthermore, by the fifth month the erythrocyte counts in all of the experimental animals had increased above the original levels. The counts remained at this elevated level for a period of four to five months. The increase in the erythrocyte counts was not accompanied by a proportionate increase in the percentage of hemoglobin, which apparently testifies to the entry into the circulating blood of erythrocytes which were less than saturated with hemoglobin. Changes in the erythrocyte content of the blood of control dogs throughout the course of the year were not regular.

The red marrow during the first month after onset of irradiation gave evidence of stimulation - in the peripheral blood there were numbers of young cells of the red cell series - reticulocytes (Fig. 2). The reaction was

especially marked in dog Metis - the strong, relatively equilibrated type. From the fifth to the ninth month - the period of marked increase in the erythrocyte level of the blood - the reticulocyte counts declined. In two of the control dogs (Byel'chik, Mak), there was a certain increase in the reticulocyte count in the first two months, but later, in all three of the control animals (Byel'chik, Mak, and Erik), the changes in the reticulocyte counts were irregular.

Very interesting and striking were the changes observed with respect to the thrombocyte counts (Fig. 3). In all dogs, a month after the onset of radiation, there was an increase in the thrombocyte counts; during the period from the second to the fifth month, the changes exhibited a fluctuant character. Beginning with the fifth month, and continuing to the tenth, an increase in the thrombocyte counts was observed in three irradiated dogs Tuzik, Metis, and Dzhul'bars). The magnitude of the increase in the thrombocyte counts varied from 121 thousand to 276 thousand per cu mm. An exception to this was seen in Ryabchik - the dog of the weak type of nervous activity, in which, after a transitory increase in the thrombocyte counts, there was a gradual but regular decline in the level of these cells by the end of the first month. In two of the control dogs, during the first four months, there was a slight increase in the thrombocyte counts, whereas later, in all three animals, the thrombocyte counts remained at the same level.

The content of leukocytes in the blood of the irradiated animals during the course of the year exhibited a marked lability, with a tendency to reduction, being especially pronounced in the dogs of the strong type (Tuzik and Metis) (Fig. 4). In the control dogs, however, during the course of 11 to 12 months, in the presence of a regular fluctuation in the changes, there was a certain increase in the leucocyte counts. These reductions of leukocyte counts in experimental animals of the strong type are due to reductions in the numbers of neutrophils and, partially, of lymphocytes. Regular changes were not seen in the absolute numbers of monocytes, basophils, and cosinophils either in the irradiated or in the control dogs.

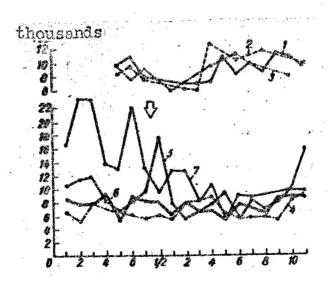


Fig. 4. Changes in the leukocyte counts.

Vertical scale represents the leukocyte counts in thousands. The other designations are the same as in Fig. 1.

We saw no degenerative changes in the cells of wither the white or red blood throughout the entire time of our investigation.

## Conclusions

- (1) Systematic observations of the morphologic composition of the blood during the period of a year in dogs subjected to total external irradiation with small doses of gamma-rays from radioactive cobalt, indicate that the changes in the hematologic indices are characterized by great lability.
- (2) Especially pronounced was the polycythemic reaction which was seen in the majority of the investigated animals during the period from the fifth to the ninth month after onset of radiation. At these same times, there was a marked increase in the number of thrombocytes.

- (3) The results of our observations afford us some basis for assuming that in animals of the strong type of higher nervous activity, during certain periods of exposure to penetrating radiation, changes in the morphologic composition of the blood are different from those seen in animals of the weak type.
- (4) During the course of the year we did not see any degenerative changes in the morphologic components of the peripheral blood in our experimental animals.

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